

What is claimed is:

1. An isolated polypeptide selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence selected from the group consisting of

5 SEQ ID NO:5 and SEQ ID NO:7,

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7,

c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7, and

10 d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7.

2. An isolated polypeptide of claim 1 comprising an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7.

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3. An isolated polynucleotide encoding a polypeptide of claim 1.

4. An isolated polynucleotide encoding a polypeptide of claim 2.

20 5. An isolated polynucleotide of claim 4 comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:6 and SEQ ID NO:8.

6. A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 3.

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7. A cell transformed with a recombinant polynucleotide of claim 6.

8. A transgenic organism comprising a recombinant polynucleotide of claim 6.

30 9. A method of producing a polypeptide of claim 1, the method comprising:

a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of

claim 1, and

- b) recovering the polypeptide so expressed.

10. A method of claim 9, wherein the polypeptide comprises an amino acid sequence

5 selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7.

11. An isolated antibody which specifically binds to a polypeptide of claim 1.

12. An isolated polynucleotide selected from the group consisting of:

10 a) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:6 and SEQ ID NO:8,

15 b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:6 and SEQ ID NO:8,

c) a polynucleotide complementary to a polynucleotide of a),

d) a polynucleotide complementary to a polynucleotide of b), and

e) an RNA equivalent of a)-d).

13. An isolated polynucleotide comprising at least 60 contiguous nucleotides of a

20 polynucleotide of claim 12.

14. A method of detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 12, the method comprising:

a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides

25 comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

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15. A method of claim 14, wherein the probe comprises at least 60 contiguous nucleotides.

16. A method of detecting a target polynucleotide in a sample, said target polynucleotide

having a sequence of a polynucleotide of claim 12, the method comprising:

- a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and
- b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

5 17. A composition comprising a polypeptide of claim 1 and a pharmaceutically acceptable excipient.

10 18. A composition of claim 17, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7.

15 19. A method for treating a disease or condition associated with decreased expression of functional PDE8, comprising administering to a patient in need of such treatment the composition of claim 17.

20 20. A method of screening a compound for effectiveness as an agonist of a polypeptide of claim 1, the method comprising:

- a) exposing a sample comprising a polypeptide of claim 1 to a compound, and
- b) detecting agonist activity in the sample.

25 21. A composition comprising an agonist compound identified by a method of claim 20 and a pharmaceutically acceptable excipient.

22. A method for treating a disease or condition associated with decreased expression of functional PDE8, comprising administering to a patient in need of such treatment a composition of claim 21.

30 23. A method of screening a compound for effectiveness as an antagonist of a polypeptide of claim 1, the method comprising:

- a) exposing a sample comprising a polypeptide of claim 1 to a compound, and
- b) detecting antagonist activity in the sample.

24. A composition comprising an antagonist compound identified by a method of claim 23 and a pharmaceutically acceptable excipient.

25. A method for treating a disease or condition associated with overexpression of functional PDE8, comprising administering to a patient in need of such treatment a composition of claim 24.

26. A method of screening for a compound that specifically binds to the polypeptide of claim 1, the method comprising:

- a) combining the polypeptide of claim 1 with at least one test compound under suitable conditions, and
- b) detecting binding of the polypeptide of claim 1 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 1.

27. A method of screening for a compound that modulates the activity of the polypeptide of claim 1, the method comprising:

- a) combining the polypeptide of claim 1 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 1,
- b) assessing the activity of the polypeptide of claim 1 in the presence of the test compound, and
- c) comparing the activity of the polypeptide of claim 1 in the presence of the test compound with the activity of the polypeptide of claim 1 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 1 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 1.

28. A method of screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:

- a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,
- b) detecting altered expression of the target polynucleotide, and
- c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

29. A method of screening for potential toxicity of a test compound, the method comprising:

a) treating a biological sample containing nucleic acids with the test compound,

b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 12 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 12 or fragment thereof,

c) quantifying the amount of hybridization complex, and

d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

30. A method for a diagnostic test for a condition or disease associated with the expression

15 of PDE8 in a biological sample, the method comprising:

a) combining the biological sample with an antibody of claim 11, under conditions suitable for the antibody to bind the polypeptide and form an antibody:polypeptide complex, and

b) detecting the complex, wherein the presence of the complex correlates with the presence of the polypeptide in the biological sample.

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31. The antibody of claim 11, wherein the antibody is:

a) a chimeric antibody,

b) a single chain antibody,

c) a Fab fragment,

d) a F(ab')<sub>2</sub> fragment, or

e) a humanized antibody.

32. A composition comprising an antibody of claim 11 and an acceptable excipient.

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33. A method of diagnosing a condition or disease associated with the expression of PDE8 in a subject, comprising administering to said subject an effective amount of the composition of claim 32.

34. A composition of claim 32, further comprising a label.

35. A method of diagnosing a condition or disease associated with the expression of PDE8 in a subject, comprising administering to said subject an effective amount of the composition of claim 34.

5        36. A method of preparing a polyclonal antibody with the specificity of the antibody of claim 11, the method comprising:

- a) immunizing an animal with a polypeptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7, or an immunogenic fragment thereof, under conditions to elicit an antibody response,
- 10      b) isolating antibodies from the animal, and
- c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which specifically binds to a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7.

15        37. A polyclonal antibody produced by a method of claim 36.

38. A composition comprising the polyclonal antibody of claim 37 and a suitable carrier.

39. A method of making a monoclonal antibody with the specificity of the antibody of claim 20 11, the method comprising:

- a) immunizing an animal with a polypeptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7, or an immunogenic fragment thereof, under conditions to elicit an antibody response,
- b) isolating antibody producing cells from the animal,
- 25      c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells,
- d) culturing the hybridoma cells, and
- e) isolating from the culture monoclonal antibody which specifically binds to a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID 30 NO:7.

40. A monoclonal antibody produced by a method of claim 39.

41. A composition comprising the monoclonal antibody of claim 40 and a suitable carrier.

42. The antibody of claim 11, wherein the antibody is produced by screening a Fab expression library.

5       43. The antibody of claim 11, wherein the antibody is produced by screening a recombinant immunoglobulin library.

44. A method of detecting a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7 in a sample, the method comprising:

- 10      a) incubating the antibody of claim 11 with the sample under conditions to allow specific binding of the antibody and the polypeptide, and  
          b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7 in the sample.

15       45. A method of purifying a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7 from a sample, the method comprising:

- 20      a) incubating the antibody of claim 11 with the sample under conditions to allow specific binding of the antibody and the polypeptide, and  
          b) separating the antibody from the sample and obtaining the purified polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:7.

25       46. A microarray wherein at least one element of the microarray is a polynucleotide of claim 13.

25       47. A method of generating an expression profile of a sample which contains polynucleotides, the method comprising:  
          a) labeling the polynucleotides of the sample,  
          b) contacting the elements of the microarray of claim 46 with the labeled polynucleotides of  
30      the sample under conditions suitable for the formation of a hybridization complex, and  
          c) quantifying the expression of the polynucleotides in the sample.

48. An array comprising different nucleotide molecules affixed in distinct physical locations on a solid substrate, wherein at least one of said nucleotide molecules comprises a first

oligonucleotide or polynucleotide sequence specifically hybridizable with at least 30 contiguous nucleotides of a target polynucleotide, and wherein said target polynucleotide is a polynucleotide of claim 12.

5        49. An array of claim 48, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 30 contiguous nucleotides of said target polynucleotide.

10      50. An array of claim 48, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 60 contiguous nucleotides of said target polynucleotide.

15      51. An array of claim 48, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to said target polynucleotide.

20      52. An array of claim 48, which is a microarray.

25      53. An array of claim 48, further comprising said target polynucleotide hybridized to a nucleotide molecule comprising said first oligonucleotide or polynucleotide sequence.

30      54. An array of claim 48, wherein a linker joins at least one of said nucleotide molecules to said solid substrate.

35      55. An array of claim 48, wherein each distinct physical location on the substrate contains multiple nucleotide molecules, and the multiple nucleotide molecules at any single distinct physical location have the same sequence, and each distinct physical location on the substrate contains nucleotide molecules having a sequence which differs from the sequence of nucleotide molecules at another distinct physical location on the substrate.

40      56. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:5.

45      57. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:7.

50      59. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID:6.

oligonucleotide or polynucleotide sequence specifically hybridizable with at least 30 contiguous nucleotides of a target polynucleotide, and wherein said target polynucleotide is a polynucleotide of claim 12.

5        49. An array of claim 48, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 30 contiguous nucleotides of said target polynucleotide.

10      50. An array of claim 48, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 60 contiguous nucleotides of said target polynucleotide.

15      51. An array of claim 48, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to said target polynucleotide.

20      52. An array of claim 48, which is a microarray.

25      53. An array of claim 48, further comprising said target polynucleotide hybridized to a nucleotide molecule comprising said first oligonucleotide or polynucleotide sequence.

30      54. An array of claim 48, wherein a linker joins at least one of said nucleotide molecules to said solid substrate.

35      55. An array of claim 48, wherein each distinct physical location on the substrate contains multiple nucleotide molecules, and the multiple nucleotide molecules at any single distinct physical location have the same sequence, and each distinct physical location on the substrate contains nucleotide molecules having a sequence which differs from the sequence of nucleotide molecules at another distinct physical location on the substrate.

40      56. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:5.

45      57. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:7.

50      59. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID:6.

55      60. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID:8.